

REMARKS

Claims 1 and 6-8 are currently pending in the application. Claims 1 and 6-8 are in independent form.

Applicants wish to express their appreciation for the courtesies extended to Applicants' representative, Amy E. Rinaldo during a telephonic interview conducted on November 11, 2005. During the telephonic interview the Examiner requested that a specific mode of administration be inserted into the independent claims. However, upon review of the application as filed, it is noted that the methods disclosed in the specification disclose numerous forms of administration including, but not limited to, interperitonealy and intravascularly. The primary purpose of the administration is to place the compounds into the body of the individual being treated. Once the compounds are in the bloodstream, or in the body, of the individual the compounds can then be distributed to all parts of the individual. When the compounds are administered and gain access to the brain, the described effect is found in the brain. Accordingly, no limitation has been inserted into the claim with regard to a specific mode of administration.

Claims 1-8 stand provisionally rejected under the judicially created doctrine of double patenting over claims 1-13 of co-pending application USSN 10/075,715. An appropriately executed terminal disclaimer is enclosed herewith, thereby overcoming the present rejection. Reconsideration is respectfully requested.

Claims 2-5 stand rejected under 35 U.S.C. § 102(b) as being anticipated by the Moskowitz patent. In order to further prosecution, claims 2-5 have been canceled without prejudice, thereby rendering the present rejection moot. Reconsideration of the rejection is respectfully requested.

Claims 2, 3, and 4 stand rejected under 35 U.S.C. § 102(b) as being anticipated by the Hindley et al. reference. Claims 2, 3, and 4 have been canceled without prejudice thereby rendering the present rejection moot. Reconsideration of the rejection is respectfully requested.

Claim 2 stand rejected under 35 U.S.C. § 102(b) as being anticipated by either the Neilsen et al. reference or the Poluha et al. reference. Claims 2 has been canceled without prejudice thereby rendering the present rejection moot. Reconsideration of the rejection is respectfully requested.

Claims 1 and 6 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the Moskowitz patent taken with the Poluha et al. reference and the Adams et al. patent. Reconsideration of the rejection under 35 U.S.C. §103(a), as being unpatentable over the Moskowitz patent, the Poluha, et al. reference, and the Adams, et al. patent is respectfully requested.

Specifically, the Office Action holds that the Moskowitz patent teaches L-arginine is an NO donor but does not *per se* teach the promotion of neural growth, and can also be administered to a stroke patient before, during, or after a stroke. The Poluha, et al. reference teaches that NO is known to result in neural outgrowth of cells.

The Office Action further holds that the Adams, et al. patent teaches systemic routes for administering NO and that NO donors can be administered to patients to reverse pathologic vascular degradation. Therefore, one skilled in the art would have known to add NO to promote neural outgrowth for treatment of stroke where neurological impairment occurs. During the telephonic interview with the Examiner we discussed that the Moskowitz patent does not disclose the ability to treat an individual post completion of stroke. The attached Declaration provides further support establishing that the Moskowitz patent could not have taught the method of the presently pending claims.

It is Hornbook Law that before two or more references may be combined to negate patentability of a claimed invention, at least one of the references must teach or suggest the benefits to be obtained by the combination. This statement of law was first set forth in the landmark case of Ex parte McCullom, 204 O.G. 1346; 1914 C.D. 70. This decision was rendered by Assistant Commissioner Newton upon appeal from the Examiner-in-Chief and dealt with the matter of combination of references. Since then, many courts have over the years affirmed this doctrine.

The applicable law was more recently restated by the Court of Appeals for the Federal Circuit in the case of ACS Hospital Systems, Inc. v. Montefiore Hospital, 732 F.2d 1572, 1577, 221 U.S.P.Q. 929 (Fed. Cir. 1984). In this case the Court stated, on page 933, as follows:

"Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. Under Section 103 teachings of references can be combined only if there is some suggestion or incentive to do so. The prior art of record fails to provide any such suggestion or incentive. Accordingly we hold that the court below erred as a matter of law in concluding that the claimed invention would have been obvious to one of ordinary skill in the art under section 103."

This Doctrine was even more recently reaffirmed by the CAFC in Ashland Oil, Inc. v. Delta Resins and Refractories, Inc., et al., 776 F.2d 281,297, 227 U.S.P.Q. 657,667. As stated, the District Court concluded:

"Obviousness, however, cannot be established by combining the teachings of the prior art to produce the claimed invention unless there was some teaching, suggestion, or incentive in this prior art, which would have made such a combination appropriate."

The Court cited ACS Hospital Systems, Inc. in support of its ruling. This Doctrine was reaffirmed in In re Deuel, 34 USPQ2d 1210 (Fed. Cir. 1995).

As discussed above, the Moskowitz patent discloses administrating an NO donor compound to a stroke patient before or up to two hours after the stroke has occurred, but does not disclose neurogenesis or new neural growth resulting from the administration of an NO donor compound.

One would not look to Poluha, et al. to improve the stroke treatment disclosed in Moskowitz. As discussed above, Poluha, et al. is not related to neurogenesis. In fact, looking at Poluha, et al. would confirm the evidence in Moskowitz that the nervous system cannot regenerate, since Poluha, et al. shows that administrating NO donors blocks cell proliferation. Neither of these references alone or combined

demonstrate that neurogenesis occurs when an NO donor compound is administered.

Adams, et al. discloses administering an anti-pressor agent such as an NO donor to remodel vasculature and is concerned with improving blood flow to arteries by increasing radial size. Adams, et al. is not at all related to neurogenesis or new neuron growth. Improving blood flow is irrelevant to neurogenesis and recovering function after a stroke. Applying the method of Adams, et al. to the invention of Moskowitz would only increase the blood flow in the stroke victim and would do nothing to promote neurogenesis.

The present application provides examples of the opposite result of Poluha, et al. – that NO donors enhance cell proliferation. The present invention also is not related to improving blood flow to arteries. The combination of either Poluha, et al. or Adams, et al. with Moskowitz would not lead to the present invention. The examples of the present invention show that the administration of NO donor compounds promotes neurogenesis and new neuron growth, and therefore the present invention is patentable over the combination of Moskowitz, Poluha, et al. and Adams, et al.

Since neither the cited references alone or in combination with knowledge in the art suggest the currently claimed invention, it is consequently respectfully submitted that the claims are clearly patentable over the combination, even if the

combination were to be applied in opposition to applicable law, and reconsideration of the rejection is respectfully requested.

Claims 7 and 8 stand rejected under 35 U.S.C. §103(a) as being unpatentable over the Moskowitz patent ('940), taken with the Poluha, et al. reference, and the Adams, et al. patent ('763), and further in view of Van Wagenen, et al (J. Neurobiology Vol. 39:2 168-185 (1999)). Specifically, the Office Action holds that Van Wagenen, et al. teaches that growth cones serve sensory and motor functions and L-arginine is a sensitizing agent. Therefore, it would have been obvious to combine the Moskowitz, Poluha, et al. and Adams, et al. teachings that administering NO effects neural growth with those of Van Wagenen, et al. Reconsideration of the rejection under 35 U.S.C. §103(a), as being unpatentable over the Moskowitz patent, the Poluha, et al. reference, the Adams, et al. patent, and the Van Wagenen, et al. reference is respectfully requested.

Van Wagenen, et al. teaches that NO donors caused an elongation of filopodia and reduction of number of filopodia on the growth cones of snail neurons. Filopodia extend from the leading edge of a growth cone, aiding in the growth cone's navigational abilities, therefore serving sensory and motor functions *for the growth cone*. The filopodia are not involved in the overall motor and sensory functions of the brain and body. Van Wagenen, et al. teaches that low concentrations of NO acts as a cue that increases a neuron's growth cone action radius by the elongation of filopodia. (p. 183) Thus, NO donors can affect the ability of a growth cone to move

toward a particular synapse to make a neuronal connection. Van Wagenen, et al. does not teach anything about neurogenesis or the recovery of function in the brain after a stroke or neural injury. There is no evidence that the mobility of existing growth cones can increase brain functionality or cognitive ability after a stroke or neural injury.

The presently pending claims are directed to increasing neural/cognitive function from neurogenesis and new neural growth. As described above, neurogenesis and new neural growth is unrelated to neurite outgrowth, wherein already existing neural growth cones navigate to associate with a particular synapse. Applying the teachings of Van Wagenen, et al. to the combination of Moskowitz, Poluha, et al. and Adams, et al. as discussed above, would only suggest that NO donors can increase growth cone mobility in a stroke victim, not that new neurons can be formed or that function can be recovered in the brain after a stroke or neural injury. Therefore, the combination of Moskowitz, Poluha, et al. and Adams, et al. in view of Van Wagenen, et al. does not suggest a method of increasing neural or cognitive function from new neural growth by the administration of NO donors.

The Office Action holds that Van Wagenen, et al. teaches that growth cones serve sensory and motor functions and L-arginine is a sensitizing agent. Therefore, it would have been obvious to combine the Moskowitz patent, the Poluha, et al. reference, and the Adams, et al. patent teachings that administering NO effects neural growth with those of the Van Wagenen, et al. reference. Reconsideration of the

rejection under 35 U.S.C. §103(a), as being unpatentable over the Moskowitz patent, the Poluha, et al. reference, the Adams, et al. patent, and the Van Wagenen, et al. reference is respectfully requested.

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The presently pending claims are directed to increasing neural/cognitive function from neurogenesis and new neural growth. As described above, neurogenesis and new neural growth is unrelated to neurite outgrowth, wherein already existing neural growth cones navigate to associate with a particular synapse. Applying the teachings of Van Wagenen, et al. to the combination of the Moskowitz

patent, the Poluha, et al. reference, and the Adams, et al. patent as discussed above, would only suggest that NO donors can increase growth cone mobility in a stroke victim, not that new neurons can be formed or that function can be recovered in the brain after a stroke or neural injury. Therefore, the combination of the Moskowitz patent, Poluha, et al. reference, and the Adams, et al. patent in view of the Van Wagenen, et al. reference does not suggest a method of increasing neural or cognitive function from new neural growth by the administration of NO donors.

Since neither the cited references alone or in combination with knowledge in the art suggest the currently claimed invention, it is consequently respectfully submitted that the claims are clearly patentable over the combination, even if the combination were to be applied in opposition to applicable law, and reconsideration of the rejection is respectfully requested.

In view of the present amendment and foregoing remarks, reconsideration of the rejections and advancement of the case to issue are respectfully requested.

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Attorney Docket No: 1059.00063

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Respectfully submitted,

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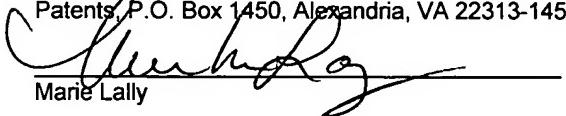
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